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Chronic respiratory symptoms and lung abnormalities among people with a history of tuberculosis in Uganda: a national survey.

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10 Chronic respiratory symptoms and lung abnormalities among people with a history of tuberculosis
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12

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33

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50 **Key points**

51 Among the general population of Uganda, ex-TB patients are at high risk of chronic cough, phlegm,
52 chest pain, haemoptysis and chest x-ray abnormalities. A history of TB was a greater predictor of
53 chronic respiratory problems than old age or smoking.

54

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56

57 **ABSTRACT**

58

59 **Background**

60 People with pulmonary tuberculosis (TB) are at risk of developing chronic respiratory disorders due
61 to residual lung damage. So far, the scope of the problem in high burden TB countries is relatively
62 unknown.

63

64 **Methods**

65 Chronic respiratory symptoms (cough and phlegm lasting >2 weeks) and radiological lung
66 abnormalities were compared between adults with and without a history of TB among the general
67 population of Uganda. Multivariable regression models were used to estimate odds ratios with
68 adjustment for age, gender, smoking, education, setting and region. Random effects models
69 accounted for village clustering effect.

70

71 **Results**

72 Of 45,293 invited people from 70 villages, 41,154 (90.9%) participated in the survey. 798 had a
73 history of TB and among them, 16% had respiratory symptoms and 41% x-ray abnormalities.
74 Adjusted odds ratios showed strong evidence for individuals with a history of TB having increased
75 risk of respiratory symptoms (OR=4.02, 95%CI: 3.25-4.96) and x-ray abnormalities (OR=17.52,
76 95%CI: 14.76-20.79); attributing 6% and 24% of the respective population risks.

77

78 **Conclusions**

79 In Uganda, a history of TB was a strong predictor of respiratory symptoms and lung abnormalities,
80 before older age and smoking. Eliminating TB disease could reduce the prevalence of chronic
81 respiratory symptoms as much as eliminating smoking.

82

84 **BACKGROUND**

85

86 Tuberculosis (TB) is the biggest cause of death from a single infectious disease resulting in an
87 estimated 10·4 million new patients and 1·3 million deaths globally in 2016.^[1] Uganda has a high
88 burden of TB with an estimated incidence of 201 new TB cases and 26 TB-related deaths per
89 100,000 population per year.^[2] Yet, TB-associated mortality and morbidity are usually only
90 captured during treatment, while post-treatment sequelae are less well documented and recognized.
91 TB disease can lead to chronic lung damage including scarring, fibrosis and cavitation, with
92 associated radiological abnormalities.^[3, 4] These lung abnormalities are the main risk factor for
93 cured TB patients to develop airflow limitations, chronic respiratory symptoms and diseases
94 including chronic obstructive pulmonary disease (COPD), bronchiectasis and aspergillosis.^[4-8]
95 People with post-TB chronic respiratory disorders can be prone to breathlessness, fatigue, physical
96 inactivity and psychosocial isolation which have negative consequences for quality of life and
97 earnings.^[9, 10]

98

99 Simultaneously, chronic respiratory diseases show an increasing global trend with COPD now
100 being the third leading cause of death. An estimated 3·2 million people died of COPD in 2015,
101 disproportionately affecting people in low- and middle-income countries where diagnosis and
102 treatment are often poor.^[11, 12] In Uganda, a recent survey in a rural district found a COPD
103 prevalence as high as 16%.^[13] Recent international surveys have confirmed that TB is an important
104 risk factor of COPD, besides smoking and air pollution.^[11, 12] A history of TB is estimated to triple
105 the risk of COPD (OR 3·05, 95%CI: 2·42-3·85) and even more in countries with a higher TB
106 incidence.^[14-17] Despite the emerging evidence on the relationship between TB and chronic lung
107 disorders, there is a lack of programmatic recommendations and interventions to identify and
108 manage patients beyond their cure of TB.^[18, 19] A systematic scoping review conducted by the
109 authors found that no international TB guidelines addressed the issue.^[20] There is a limited number

110 of studies on the prevalence of post-TB lung disorders, especially from Sub-Saharan Africa.^[16, 17, 21]
111 One study from South Africa assessed post-TB chronic bronchitis (cough and phlegm ≥ 3 months)
112 through a national survey in 2004, but did not include other respiratory symptoms or chest x-ray
113 abnormalities.^[22] Few studies in general have related structural lung damage to respiratory
114 symptoms.^[4] To contribute to the evidence on post-TB lung disorders, this study assessed a range of
115 chronic respiratory symptoms and radiological abnormalities among the general population of
116 Uganda using data from the most recent national TB prevalence survey.

117

118 **METHODS**

119

120 **Study design and population**

121 This study used data from the national TB prevalence survey of Uganda conducted in 2014-2015 by
122 the Ministry of Health together with Makerere University, WHO and Centers for Disease Control
123 and Prevention.^[23] In the original survey, a national representative sample was obtained using the
124 entire country as the sampling frame and villages as the sampling units. Villages were stratified by
125 rural and urban settings and a total of 70 villages with between 550 and 680 eligible respondents
126 were selected with probability proportionate to population size. All households in a selected village
127 were included. All consenting permanent residents and those visiting the residence since more than
128 two weeks aged 15 years and above were eligible.

129

130 Ethical approval of the original survey was granted by the Institutional Review Boards of the
131 Higher Degree Research and Ethics Committee (HDREC) at the Makerere University School of
132 Public Health and the Uganda National Council of Science and Technology (UNCST), under
133 reference number IRB00011353.

134

135 **Data collection**

136 Data for the original household survey was collected from October 2014 to July 2015. Participants
137 were interviewed with a questionnaire on demographics, clinical symptoms, smoking behaviour,
138 and current and past TB treatment (see Box 1). Subsequently, all people received a chest x-ray to
139 assess lung abnormalities as per WHO guidelines. The films were read by radiology consultants
140 from the national lung hospital. Participants with cough for two weeks or more and/or an abnormal
141 chest x-ray were asked to provide two sputum samples for bacteriological tests for active TB
142 disease (smear microscopy, GeneXpert, culture). Participant data from questionnaires, chest x-rays
143 and laboratory tests were entered, cleaned, verified and anonymised in an electronic database using
144 EpiInfo version 3.51.

145

146 For the present study, people with current TB were excluded, i.e. those who reported to be taking
147 anti-TB drugs or who were diagnosed with active TB disease during the survey. People with a
148 history of TB were those who self-reported to ever have been treated for TB in their lifetime but did
149 not have current TB disease. Regions represented statistical groupings of districts without
150 administrative or political status as used in the 2002 Uganda Census.^[24]

151

152 **Outcomes**

153 *Respiratory symptoms*

154 Respiratory symptoms were recorded as self-reported presence or absence and duration in days of:
155 cough; phlegm; haemoptysis; and chest pain. A composite binary outcome for chronic respiratory
156 symptoms (presence or absence) was constructed based on cough and phlegm: people who reported
157 both cough and phlegm of two weeks or more were classified as having chronic respiratory
158 symptoms. Haemoptysis was not included in the composite outcome because this is a rare symptom
159 of severe chronic respiratory disease. Chest pain, although potentially linked to respiratory
160 problems, is not a distinguishing symptom of chronic lung disease.^[9]

161

162 *Lung abnormalities*

163 Radiological lung abnormalities were based on chest x-ray reports, which for this analysis were
164 converted from a categorical to a binary variable, i.e.: reports of inactive/healed TB, suggestive
165 active TB disease and other lung abnormalities, whether or not they were thought to be consistent
166 with TB, were regrouped as presence of lung abnormalities; normal readings and extra-pulmonary
167 abnormalities were regrouped as absence of lung abnormalities; poor x-ray/not read and missing
168 readings were recoded as missing.

169

170 **Statistical analysis**

171 The proportion of chronic respiratory symptoms and radiological lung abnormalities was presented
172 for the overall study population and for people with and without a history of TB. This study had
173 90% power at a two-sided 5% significance level to detect a proportional difference of 2.5% for the
174 main outcomes between people with and without a history of TB. Crude odds ratios of the
175 association between past TB and both outcomes were calculated with 95% confidence intervals and
176 Chi-square tests. Multivariable logistic regression models were used to adjust for age, gender,
177 smoking, education, region and setting. Multi-collinearity between these variables was assessed
178 using variance inflation factors (VIF) and variables were dropped from the model if $VIF > 10$.
179 Adjustment for village clustering was done using a random effects model. Effect modifiers were
180 included in the final model if the effect on outcomes varied dramatically (i.e. reverse direction)
181 across variable subgroups. Finally, population attributable risk fractions were calculated for the two
182 main outcomes using standard formulas. Statistical analyses were performed using STATA version
183 SE14.

184

185 Sensitivity analyses were performed to explore the impact of different outcome definitions. First,
186 we estimated the odds ratios for chronic respiratory symptoms using a three-month cut-off point
187 rather than two weeks, as GOLD guidelines do not specify the minimum duration of respiratory

188 symptoms for classification of e.g. COPD.^[9] Secondly, we estimated the odds ratio of radiological
189 lung abnormalities reclassifying people with 'inactive/healed TB' as having no lung abnormalities,
190 since some ex-TB patients could have for example calcified lymph nodes without ever developing
191 respiratory disorders.

192

193 **RESULTS**

194

195 Of 45,293 eligible individuals, 41,154 (90.9%) received symptoms screening and/or chest x-ray
196 scans. After excluding 205 people with current TB, 40,949 people remained of whom 204 (<1%)
197 had missing chest x-ray data (respiratory symptom data was complete). Table 1 shows the
198 characteristics of the study population. A total of 798 out of 40,949 people (1.9%) reported a
199 history of TB and 40,151 (98.1%) reported no history of TB. People with a history of TB were
200 more often male (52.9%), living in the north (31.3%) or central region (35.3%), living in urban
201 settings (47.1%), past (20.9%) or current smokers (10.0%), and older than people without a history
202 of TB.

203

204 Table 2 shows the proportion of people with chronic respiratory symptoms (individual and
205 composite) and radiological lung abnormalities. As many as 21% of the general population reported
206 chest pain. Among people with a history of TB, 16% reported cough and phlegm, 41% had lung
207 abnormalities and 9% had both. A history of TB was crudely associated with cough and phlegm
208 (OR 4.95, 95%CI: 4.06-6.05), as well as lung abnormalities (OR 21.79, 95%CI: 18.60-25.53).
209 Although symptoms and lung damage were highly correlated ($p < 0.0001$), the majority of people
210 with lung abnormalities did not report cough and phlegm (78%; 253/326), and some with symptoms
211 had no lung abnormalities (41%; 50/123). Still, people with past TB and lung abnormalities had
212 2.41 (95%CI: 1.62-3.58) times the odds of respiratory symptoms than those with no x-ray
213 abnormalities.

214

215 Age, smoking, gender, region, setting and education were included as potential confounders in a
216 multivariable logistic regression model. None of the variables showed multi-collinearity (all
217 VIF<1.2). Table 3 shows that after adjusting for these factors, as well as for village clustering
218 effect, there was still a significant association between a history of TB and respiratory symptoms.
219 People with a history of TB had 4.02 (95%CI: 3.25-4.96; $p<0.001$) times the odds of chronic cough
220 and phlegm than people without a history of TB. The odds of having respiratory symptoms also
221 increased with older age and smoking, while living in the western region of the country and having
222 a higher education decreased the odds. The within-village correlation coefficient ($\rho=0.041$,
223 95%CI: 0.026-0.064, $p<0.001$) indicated that people living within the same village were indeed
224 more similar than people living in different villages.

225

226 Table 4 shows that after adjusting for all variables and village clustering effect, people with a
227 history of TB had 17.52 (95%CI:14.76-20.79) times the odds of lung abnormalities than people
228 without a history of TB. The village clustering effect was again significant ($\rho=0.020$, 95%CI:
229 0.011-0.036, $p<0.001$). While the odd ratio of lung abnormalities varied widely across age groups
230 (LRT $p=0.0001$), from 27.34 (95%CI: 16.49-45.34) among 15-24 year olds to 8.18 (95%CI: 5.11-
231 13.11) among 65+ year olds, age did not actually reverse the effect of TB history on lung
232 abnormalities and was therefore not included as effect modifier in the final model. Besides a history
233 of TB, the odds of having lung abnormalities increased with older age and past or current smoking,
234 while living in the western region of the country and higher education decreased the odds. Women
235 had only half the odds of having lung abnormalities than men.

236

237 A history of TB attributed an estimated 6% of the population's risk of chronic respiratory symptoms
238 and 24% of the risk of radiological lung abnormalities. In comparison, older age (65+ years)
239 imposed the largest population risk on both outcomes (14% and 42%, respectively), while current

240 smoking had a similar impact on respiratory symptoms (7%) and a much smaller impact on lung
241 abnormalities (5%) than a history of TB.

242

243 A sensitivity analysis around chronic respiratory symptoms showed that using a cut-off point of
244 three months rather than two weeks actually increased the crude odds ratio from 4.95 to 7.54
245 (95%CI: 5.14-11.07) and the fully-adjusted odds ratio from 4.02 to 5.19 (95%CI: 3.43-7.84),
246 which suggested a stronger impact of a history of TB on long-term rather than short-term
247 respiratory symptoms. A sensitivity analysis around radiological lung abnormalities showed that
248 excluding people with 'inactive/healed TB' on chest x-ray would reduce the crude odds ratio from
249 21.79 to 8.67 (95%CI: 7.21-10.43) and the fully-adjusted odds ratio from 17.52 to 5.87 (95%CI:
250 4.81-7.15). This was driven by the association between a history of TB and radiological signs of
251 previous TB disease. Further inspection revealed that 74% of people with 'inactive/healed TB' had
252 atelectasis (lung collapse) and 42% had fibrosis, both commonly associated with respiratory
253 disorders, thus excluding them would underestimate the effect of a history of TB on lung
254 abnormalities.

255

256 **DISCUSSION**

257

258 This study assessed the scope of post-TB chronic respiratory symptoms and lung abnormalities
259 among the general population of Uganda and found that people with a history of TB had four times
260 the odds of having chronic respiratory symptoms and 18 times the odds of radiological lung
261 abnormalities compared to people without a history of TB. Chronic cough, phlegm, chest pain and
262 haemoptysis were all significantly more prevalent among people with than without a history of TB.
263 At individual level, a history of TB was a very strong predictor of respiratory problems even before
264 older age and smoking. At population level, a history of TB was at par with smoking and only
265 surpassed by old age in terms of attributable risk. Our sensitivity analyses showed that even when

266 chronic symptoms and lung abnormalities were defined more conservatively, strong evidence for an
267 impact of past TB as a risk factor remained. These findings are consistent with a previous study
268 from South Africa, which found odds ratios for chronic bronchitis of 4·9 (95%CI:2·6-9·1) for men
269 and 6·6 (95%CI:3·7-11·7) for women with past TB.^[22] Those findings may have been slightly
270 overestimated as the study did not exclude people with active TB disease. Most other studies on
271 respiratory symptoms or lung abnormalities have been conducted in occupational or clinical settings
272 and were less comparable. This is the first study to report on the national proportion of post-TB
273 lung abnormalities and compare it with respiratory symptoms. The fact that the majority of people
274 with lung abnormalities did not report respiratory symptoms indicates that lung damage, although
275 doubling the risk, does not always lead to respiratory disease.

276

277 Men had almost twice the odds of lung abnormalities than women after controlling for other factors
278 including TB history and smoking. This warrants further exploration as we are not aware of any
279 studies reporting a similar finding. Occupational exposure could be higher in men, but would likely
280 be outweighed by women being more exposed to household air pollution. Delays to diagnosis of
281 TB, potentially leading to increased lung damage, also tend to be higher among women.^[25] People
282 with higher levels of education were less prone to post-TB problems possibly because they were on
283 average wealthier, had better access to health services, and less often used biomass fuel for cooking.
284 People living in the western region of Uganda had reduced risks, which might be due to
285 environmental, cultural or genetic variations that can be explored in further studies. Older age
286 increases the risk of respiratory disorders because of deterioration of the lungs over a lifetime and
287 cumulative lung damage resulting from environmental exposures and other lung insults. Smoking is
288 known to be the most common cause of chronic airflow obstruction in high income countries.^[26]
289 Interestingly, this study has brought to light that eliminating TB disease in the population of
290 Uganda could result in at least as large a reduction of chronic respiratory symptoms as eliminating
291 smoking.

292

293 The strength of this study was the large, nationally representative sample of over 40,000 people.
294 The study population was similar to the general population of Uganda as measured by the 2014
295 Census in terms of gender (51% females), age (5% 65+ years) and education (19% without formal
296 education).^[27] The findings are therefore likely to be generalizable to the whole country and to other
297 countries with similar TB epidemiology and demographics. This study also had some limitations.
298 First, this study was not able to control for potential confounding by household smoke exposure,
299 outside air pollution, occupational exposure to e.g. dust or silica, diabetes and HIV status. Although
300 rural/urban setting could partly serve as proxy for inside/outside air pollution and occupational
301 exposure, positive confounding by these factors cannot be excluded. Secondly, there was a risk of
302 recall bias due to the fact that TB history and respiratory symptoms were self-reported and not
303 verified by clinical assessments or historical records. People with either of these may remember and
304 report the presence of the other more actively, which could potentially have slightly overestimated
305 our associations. Thirdly, there may have been a small risk of selection bias as 9% of the study
306 population was excluded due to missing data. However, since the excluded group was on average
307 younger, including them would likely have increased the association between a history of TB and
308 lung abnormalities. Lastly, there was a risk of survival bias as only those people who survived
309 longer post-TB will have been included in the survey and those might be the ones with milder
310 respiratory problems. If this study missed some people with severe chronic lung disorders due to
311 premature mortality, then our already strong associations would have been underestimated.
312 Future cohort studies should evaluate the potential effect of time since last TB treatment and
313 potential confounders such as indoor and outdoor air pollution and co-morbidities. Future
314 population based studies that enquire about chronic respiratory symptoms should also include
315 measures of lung function (spirometry), dyspnoea and wheeze in order to diagnose disorders like
316 COPD and bronchiectasis.

317

318 While post-TB chronic lung disorders can primarily be reduced by adequate and timely treatment
319 and prevention of active TB disease, it is equally imperative to monitor and manage respiratory
320 problems after cure of TB. People at risk of chronic respiratory problems should be identified as
321 early as possible in order to optimize prognosis and treatment outcomes, for example by offering
322 clinical symptom assessment, chest x-ray scans and lung function tests immediately or a few
323 months after being cured of TB. They are likely to benefit most from interventions including
324 smoking cessation, patient education for self-management, pulmonary rehabilitation and
325 bronchodilator therapy.^[9, 28] The tremendous expense and disability associated with chronic lung
326 diseases in North America and Europe has important implications for the future of low resource
327 countries like Uganda.^[29] Even though international guidance is lacking, Uganda has very recently
328 included the issue of post-TB lung disorders into its national TB programme guidelines. Also, a
329 preliminary study of pulmonary rehabilitation showed major improvements in dyspnoea, exercise
330 capacity and chest pains among ex-TB patients.^[30] It is important for more high burden TB
331 countries and international policy makers and researchers to consider and address the issue of post-
332 TB lung disorders if we are to reduce overall TB-related morbidity and mortality.

333

334

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342

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347

348 **Conflict of interest**

349 RJ has received personal fees from Astra Zeneca, Boehringer Ingelheim, Chiesi, GSK and Novartis,
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Table 1. Characteristics of the study population and among people with and without a history of TB among the general population of Uganda in 2014-2015

Demographics	Categories	Total (n=40,949)	History of TB (n=798)	No history of TB (n=40,151)	Crude association	Chi- square test
		<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>	<i>Odds ratio (95% CI)</i>	<i>p-value</i>
Age	15-24 years	14738 (35.99)	109 (13.66)	14629 (36.43)	1.00	-
	25-34 years	10494 (25.63)	170 (21.30)	10324 (25.71)	2.21 (1.73, 2.82)	<0.0001
	35-44 years	6785 (16.57)	175 (21.93)	6610 (16.46)	3.55 (2.79, 4.52)	<0.0001
	45-54 years	4246 (10.37)	179 (22.43)	4067 (10.13)	5.91 (4.64, 7.53)	<0.0001
	55-64 years	2203 (5.38)	79 (9.90)	2124 (5.29)	4.99 (3.72, 6.70)	<0.0001
	65+ years	2483 (6.06)	86 (10.78)	2397 (5.97)	4.82 (3.61, 6.42)	<0.0001
Gender	Male	17340 (42.35)	422 (52.88)	16918 (42.14)	1.54 (1.34, 1.77)	<0.0001
	Female	23609 (57.65)	376 (47.12)	23233 (57.86)	1.00	-
Education ^a	None	6959 (16.99)	177 (22.18)	6782 (16.89)	1.13 (0.84, 1.52)	0.423
	Primary	19780 (48.30)	353 (44.24)	19427 (48.38)	0.79 (0.60, 1.04)	0.087
	Senior 1-4	9897 (24.17)	173 (21.68)	9724 (24.22)	0.77 (0.57, 1.04)	0.083
	Senior 5-6	1655 (4.04)	35 (4.39)	1620 (4.03)	0.93 (0.61, 1.42)	0.752
	Tertiary	2655 (6.48)	60 (7.52)	2595 (6.46)	1.00	-
Region ^b	Central	13876 (33.89)	282 (35.34)	13594 (33.86)	1.47 (1.19, 1.82)	0.0003
	East	8960 (21.88)	136 (17.04)	8824 (21.98)	1.09 (0.86, 1.39)	0.466
	North	8752 (21.37)	250 (31.33)	8502 (21.18)	2.09 (1.69, 2.59)	<0.0001
	West	9360 (22.86)	130 (16.29)	9230 (22.99)	1.00	-
Setting	Rural	23705 (57.89)	422 (52.88)	23283 (57.99)	1.00	-
	Urban	17244 (42.11)	376 (47.12)	16868 (42.01)	1.23 (1.07, 1.42)	0.004
Smoking ^c	Never smoked	35290 (86.19)	551 (69.05)	34739 (86.53)	1.00	-
	Past smoker	2674 (6.53)	167 (20.93)	2507 (6.24)	4.20 (3.51, 5.02)	<0.0001
	Current smoker	2979 (7.28)	80 (10.03)	2899 (7.22)	1.74 (1.37, 2.21)	<0.0001

^a Education level: missing for 3 out of 40,949 participants (0.007%)

^b Region as per 2002 Uganda population and housing census ^[24]: missing for 1 out of 40,949 participants (0.002%)

^c Smoking: missing for 6 out of 40,949 participants (0.01%)

448 **Table 2. Proportion and unadjusted crude associations between having a history of TB and**
449 **chronic respiratory proportion among the general population of Uganda in 2014-2015**

Outcomes	Categories	Total (n=40949)	History of TB (n=798)	No history of TB (n=40151)	Crude association	Chi-square test
		<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>	<i>Odds ratio (95% CI)</i>	<i>p-value</i>
Cough	Yes	2610 (6.37)	155 (19.42)	2455 (6.11)	3.70 (3.09, 4.43)	<0.0001
>2 weeks	No	38339 (93.63)	643 (80.58)	37696 (93.89)	1.00	--
Phlegm	Yes	1692 (4.13)	129 (16.17)	1563 (3.89)	4.76 (3.91, 5.79)	<0.0001
>2 weeks	No	39257 (95.87)	669 (83.83)	38588 (96.11)	1.00	--
Haemoptysis	Yes	112 (0.27)	17 (2.13)	95 (0.24)	9.18 (5.45, 15.46)	<0.0001
>2 weeks	No	40837 (99.73)	781 (97.87)	40056 (99.76)	1.00	--
Chest pain	Yes	8578 (20.95)	257 (32.21)	8321 (20.72)	1.82 (1.56, 2.11)	<0.0001
>2 weeks	No	32371 (79.05)	541 (67.79)	31830 (79.28)	1.00	--
Chest x-ray results	Normal	38,421 (93.8)	450 (56.39)	37971 (94.57)	N/A	N/A
	Inactive/healed TB	265 (0.7)	165 (20.68)	100 (0.25)		
	Extra-pulmonary abnormalities	758 (1.9)	17 (2.13)	741 (1.85)		
	Active TB diseases suggestive	146 (0.4)	56 (7.02)	90 (0.22)		
	Other findings consistent with TB	294 (0.7)	44 (5.51)	250 (0.62)		
	Other findings not consistent with TB	861 (2.1)	61 (7.64)	800 (1.99)		
	Poor x-ray/not read	56 (0.1)	1 (0.13)	55 (0.14)		
	Missing	148 (0.4)	4 (0.50)	144 (0.36)		
Main outcomes						
Cough and phlegm >2 weeks ^a	Yes	1562 (3.81)	124 (15.54)	1438 (3.58)	4.95 (4.06, 6.05)	<0.0001
	No	39387 (96.19)	674 (84.46)	38713 (96.42)	1.00	--
Radiologic al lung abnormalities ^b	Yes	1566 (3.84)	326 (41.11)	1240 (3.10)	21.79 (18.60, 25.53)	<0.0001
	No	39179 (96.16)	467 (58.89)	38712 (96.90)	1.00	--

450 ^a Composite outcome for respiratory symptoms, combining people with cough and phlegm lasting 14 days or more

451 ^b Combining people with inactive/healed TB, active TB diseases, or other lung conditions whether consistent or not
452 consistent with TB; missing for 204 participants (<1%)

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454

455 **Table 3. Multivariable logistic regression model for the association between a history of TB**
456 **and respiratory symptoms adjusted for confounding and clustering**

Variables included in the final model for COUGH AND PHLEGM > 2 WEEKS	Fully-adjusted	Wald test
	association <i>Odds ratio (95% CI)</i>	<i>p-value</i>
History of TB	4.02 (3.25, 4.96)	<0.001
Age group (15-24 years)	--	--
25-34 years	1.29 (1.10, 1.52)	0.002
35-44 years	1.48 (1.24, 1.75)	<0.001
45-54 years	1.75 (1.46, 2.11)	<0.001
55-64 years	1.93 (1.55, 2.41)	<0.001
65+ years	3.75 (3.10, 4.53)	<0.001
Smoking (never smoked)	--	--
Past smoker	1.48 (1.24, 1.77)	<0.001
Current smoker	2.00 (1.70, 2.36)	<0.001
Region ^a (central)	--	--
East	0.99 (0.74, 1.32)	0.943
North	1.11 (0.83, 1.47)	0.482
West	0.56 (0.42, 0.75)	<0.001
Setting (rural)	--	--
Urban	0.86 (0.69, 1.07)	0.172
Education (no education)	--	--
Primary	0.74 (0.65, 0.85)	<0.001
Senior 1-4	0.53 (0.45, 0.64)	<0.001
Senior 5-6	0.35 (0.23, 0.54)	<0.001
Tertiary	0.35 (0.26, 0.49)	<0.001
Gender (male)	--	--
Female	0.90 (0.80, 1.01)	0.087
Village clustering effect	<i>Rho (95% CI)</i>	<i>LRT ^b p-value</i>
Correlation coefficient	0.041 (0.026, 0.064)	<0.001

457 ^a Region as per 2002 Uganda population and housing survey ^[24]

458 ^b LRT; likelihood ratio test

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460

461 **Table 4. Multivariable logistic regression model for the association between a history of TB**
462 **and radiological lung abnormalities adjusted for confounding and clustering**

Variables included in the final model for RADIOLOGICAL LUNG ABNORMALITIES	Fully-adjusted association	Wald test
	<i>Odds ratio (95% CI)</i>	<i>p-value</i>
History of TB	17.52 (14.76, 20.79)	<0.001
Age group (15-24 years)	--	--
25-34 years	1.90 (1.54, 2.34)	<0.001
35-44 years	3.20 (2.60, 3.94)	<0.001
45-54 years	4.85 (3.92, 5.99)	<0.001
55-64 years	6.74 (5.34, 8.52)	<0.001
65+ years	13.16 (10.61, 16.32)	<0.001
Smoking (never smoked)	--	--
Past smoker	1.43 (1.22, 1.68)	<0.001
Current smoker	1.66 (1.41, 1.95)	<0.001
Region ^a (central)	--	--
East	0.93 (0.76, 1.13)	0.474
North	0.94 (0.77, 1.13)	0.498
West	0.73 (0.60, 0.88)	0.001
Setting (rural)	--	--
Urban	1.09 (0.94, 1.26)	0.263
Education (no education)	--	--
Primary	0.87 (0.75, 1.00)	0.048
Senior 1-4	0.70 (0.58, 0.85)	<0.001
Senior 5-6	0.48 (0.31, 0.73)	0.001
Tertiary	0.72 (0.55, 0.94)	0.018
Gender (male)	--	--
Female	0.47 (0.42, 0.54)	<0.001
Village clustering effect	<i>Rho (95% CI)</i>	<i>LRT ^b p-value</i>
Correlation coefficient	0.011 (0.0045, 0.025)	0.001

463 ^a Region as per 2002 Uganda population and housing survey ^[24]

464 ^b LRT; likelihood ratio test

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